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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/926,554

11/19/2001

Enrico Di Salle

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06/24/2005

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER

JIANG, SHAOJIA A

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 06/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/926,554

Applicant(s)

SALLE ET AL.

Examiner

Shaojia A. Jiang

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2004 and 04 October 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 50-82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 50-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5/20/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 12, 2004 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed April 12, 2004, and amendment and response to the Final Office Action (dated June 2, 2004), filed October 4, 2004 wherein claims 24, 28, 30-36, 40, 42-43, and 46-49 are cancelled, and claims 50-82 are newly submitted. Claims 25-27, 29, 37-39, 41, and 44-45 are cancelled previously. Thus, all previous pending claims are cancelled.

Currently, claims 50-82 are pending in this application and under examination on the merits.

The following is new rejection(s) necessitated by Applicant's amendment filed on October 4, 2004, wherein all original claims are cancelled and the limitations in the new claims have been changed. Therefore, all rejections of record in the previous Office Action June 2, 2004 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51, 62 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 51, 62 and 73 recite "two antineoplastic agents". There is insufficient antecedent basis for this limitation in the claim since it is unclear as to which are "two antineoplastic agents" and whether these "two antineoplastic agents" are epirubicin and docetaxel recited in the independent claims or something else.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 50-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al. (US 4808616, PTO-892) in view of Tognella et al. (4,871,528, of record) and Shashoua et al. (5,795,909 of record).

Buzzetti et al. discloses that 6-methyleneandrosta-1,4-diene-3,17-dione (see col.2 line 29-30), having structural formula (I) therein(col.1 line 50-59), also known as exemestane or FCE 24304, is known to be useful in the treatment of hormone-dependent cancers such as breast, endometrial, ovarian cancers in mammals (see abstract, col. lines 5-14). Buzzetti et al. also discloses that the effective amount of exemestane or FCE 24304 is about 10 to about 150-200 mg/day which is within the claimed range herein.

Buzzetti et al. does not expressly disclose the employment of exemestane in combination with the instant antineoplastic agent, epirubicin or docetaxel in pharmaceutical compositions and methods for treating breast cancer in humans and lowering the side effects in humans.

Tognella et al. discloses mono- or polychemotherapy against tumors including breast cancer, thus avoiding dangerous side-effects and increasing the long term survival rates (see abstract). Tognella et al. discloses that the known anti-tumor agents, epirubicin (the anthracycline compound, see col.3 lines 50-57) and other known antineoplastic agents (e.g., cyclophosphamide, methotrexate, etoposide, and 5-fluorouracil), in combination, or in combination with reduced glutathione (GSH), is useful in a composition and a method of treating breast cancer in humans and lowering the side effects in humans caused by breast cancer therapy with anti-tumor agents. See abstract, col. 1 lines 20-38. Tognella et al. further discloses the effective amounts of the active agents in a composition to be administered for treating breast cancer in humans to produce synergistic effects (see col.4 lines 21-25 and 42-54, Table at col.5 lines 57-

63, Table 1-4 at col.10-12) or surprising results against tumors by polychemotherapy (see abstract).

Shashoua et al. discloses that the instant preferred antineoplastic agents such as paclitaxel, docetaxel, edatrexate, epirubicin, 5-fluorouracil, gemcitabine, irinotecan, mitoxantrone and topotecan, and the instant preferred aromatase inhibitors such as anastrozole, fadrozole, letrozole, vorozole and exemestane, are known to be useful in the treatment of cancers, tumors or proliferative disorders including breast cancer (see Fig. 27) and reducing side-effects. See abstract, col.1 lines 45-46 and col.30 line 48 to col.32.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ exemestane in combination with the instant antineoplastic agent, epirubicin or docetaxel in pharmaceutical compositions and methods for treating breast cancer in humans and lowering the side effects in humans.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ exemestane in combination with the instant antineoplastic agent, epirubicin or docetaxel in pharmaceutical compositions and methods for treating breast cancer in humans and lowering the side effects in humans, since the instant antineoplastic agents such as epirubicin and docetaxel, and exemestane, alone and/or in combination, are known to be useful in pharmaceutical compositions and methods for treating breast cancer in humans and/or lowering the side effects in humans based on the prior art.

Therefore, one of ordinary skill in the art would have reasonably expected that combining exemestane and epirubicin or docetaxel in pharmaceutical compositions to be administered, both known useful for the same purpose, i.e., treating breast cancer, would improve the therapeutic effects for treating the same disorder, and/or would produce additive therapeutic effects in treating the same. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose; idea of combining them flows logically from their having been individually taught in prior art.

Moreover, polychemotherapy against tumors is known to avoid dangerous side-effects and increasing the long term survival rates and producing synergistic effects or surprising results against tumors including breast cancer in humans according to Tognella et al. Thus, the teachings of Tognella et al. in regard to the combination chemotherapies for breast cancer using the instant agents have also provided the motivation to make the present invention.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active agents in the composition because the optimization of known effective amounts of known active agents to be administered based on the prior art, is considered well within the skill of artisan. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's arguments filed October 4, 2004 with respect to the rejection made under 35 U.S.C. 103(a) of record in the previous Office Action dated June 2, 2004 have been fully considered but are moot in view of the new ground(s) of rejection above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 50-82 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-53 of copending Application No. 10/363,935.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending Application is drawn to a pharmaceutical compositions and methods for chemopreventing or controlling the growth of estrogen

dependent cancers comprising exemestane in combination with the instant antineoplastic agents such as, a taxane compound, docetaxel, or an anthracycline compound, epirubicin.

The claims of the instant application are drawn to the employment of exemestane in combination with the instant antineoplastic agent, epirubicin or docetaxel in pharmaceutical compositions and methods for treating breast cancer in humans and lowering the side effects in humans.

Thus, the instant claims are seen to be obvious over the claims 6-53 of copending Application No. 10/363,935.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.


In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1617

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
June 16, 2005